REMARKS

The Present Invention

The present invention pertains to a composition comprising an interluekin-2 receptor associated polypeptide, wherein the polypeptide is reactive with a monoclonal antibody produced by the hybridoma PTA-82, and methods of purifying the same.

The Pending Claims

Claims 1, 3-5, 9-15, 22 and 23 are currently pending. Claims 1, 3-5, 22 and 23 are directed to compositions comprising interleukin-2 receptor associated polypeptides, which are recognized by monoclonal antibodies produced by the hybridoma PTA-82. Claims 9-15 are directed to methods of purifying the subject interleukin-2 receptor associated polypeptides.

Amendments to the Claims

Claim 1 has been amended to recite the molecular weight limitation previously presented in original claim 2, which is now canceled. Additionally, claim 1 has been amended to recite that the molecular weight of the interleukin-2 receptor associated polypeptide is determined using SDS-PAGE as supported by the specification at, for example, page 26, line 27. Claim 3 has been amended to be independent, incorporating the limitations of original claim 1, except for the specific molecular weight of the interleukin-2 receptor associated polypeptide recited therein and the method used to determine the molecular weight as supported by the specification, at for example, page 26, line 27. Claim 9 has been amended to recite the proper antecedent basis, "polypeptide" rather than "protein" in accordance with Office's suggestion and as supported by the specification at, for example, page 26, line 10. Claim 12 has been amended to recite "interleukin-2 receptor associated polypeptide" rather than "ILRAP" as suggested by the Office and as supported by the specification at, for example, page 26, lines 10, 18 and 19. Claim 13 has been amended to recite the word "receptor" to have the correct antecedent basis, as suggested by the Office and as supported by the specification at, for example, page 27, lines 30-32. Furthermore, claim 13 has been amended to recite "interleukin-2Rβ subunits," rather than "interleukin β subunits." This claim amendment is supported by the specification at, for example, page 26, line 24. Claims 6-8, 16-18, and 19-21 have been canceled as being drawn to a non-elected invention. Applicants reserve the right to pursue any canceled subject matter in a continuation, continuation-in-part, divisional application, or other application. Cancellation of any subject matter should not be construed as abandonment of that subject matter. Claims 22 and 23 are new, depend from claim 3, and recite limitations identical to original claims 4

and 5, other than the claim from which they depend. New claims 22 and 23 are supported by the specification at, for example, page 33, lines 12-18. Accordingly, no new matter has been added by way of these amendments.

Summary of the Office Action

Claims 1-5 and 9-15 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. Claims 1-4 and 9-15 have been rejected under 35 U.S.C. § 102(b), as allegedly anticipated by, or, in the alternative, allegedly obvious under 35 U.S.C. § 103(a) in view of Cerretti et al. (EP 0 162 699), and as allegedly evidenced by Colamonici et al. (J. Immunol., 145:155-160 (1990)). Claims 1-5, 9, 10 and 13-15 have been rejected under 35 U.S.C. § 102(b), as allegedly anticipated by, or, in the alternative, allegedly obvious under 35 U.S.C. § 103(a) in view of Colamonici et al. Reconsideration of the pending claims is respectfully requested.

Discussion of the Section 112, Second Paragraph, Rejection

Claims 1, 3-5, and 9-15 have been rejected as allegedly indefinite. Claim 1 is allegedly indefinite for not defining the subject polypeptide by its structural, physical or chemical features, for reciting the term "composition" as identifying a single component, reciting the term "peptide" without proper antecedent basis, and for using the term "reactive," which, according to the Office, is unclear. Likewise, Claims 3-5 and 15 are allegedly indefinite for reciting the term "composition." Claim 2, the limitations of which are now incorporated into claim 1, is allegedly indefinite for failing to specify how the molecular weight of the subject polypeptide is determined. Claim 9 is allegedly indefinite for being incomplete for omitting essential elements, for improper antecedent basis for the word "protein", and for not clearly identifying the antibody being used in the method. Similarly, claims 10 and 11 are allegedly indefinite for omitting essential elements. Claim 10 allegedly is also indefinite for reciting that cells can be contacted after being solubilized. Claim 12 is allegedly indefinite for improper antecedent basis of the term "ILRAP." Claim 13 is allegedly indefinite because the term "interleukin β subunits" is unclear, why such cells would be expected to express the polypeptide of interest, and for improper antecedent basis. The rejection is respectfully traversed for the reasons set forth below.

Claim 1 has been amended to recite physical features (molecular weight) of the subject polypeptide and how it is determined, and to recite the proper antecedent basis, "associated polypeptide." The Office alleges that claim 1 is indefinite for reciting a single component to define the term "composition." There is no requirement that a claimed composition comprises more than one element. Additionally, Applicants direct the Office's

attention to the transitional phrase of claim 1, "comprising." The transitional phrase "comprising" is inclusive or open-ended and does not exclude additional, unrecited elements. *See M.P.E.P. § 2111.03*. Furthermore, "comprising" is used to mean that the named elements are essential, but other elements may be added to form a composition within the scope of the claim. *Id.* In claims 1, 3-5, and 15, the essential element of the composition is an interleukin-2 receptor associated polypeptide, and thus, it is recited therein. However, the fact that a second essential element is not required or recited does not prevent Applicants from claiming a composition, as suggested by the Office, since a non-essential element can fall within the scope of the claim without being recited in the claim itself due to the use of the transitional phrase "comprising." Therefore, claims 1, 3-5 and 15 are not indefinite for use of the term "composition" even though only a single essential element is recited to describe a composition.

Additionally, with respect to claim 1, the Office alleges that the term "reactive" is unclear, because it is not clear what Applicants intended. Applicants respectfully disagree with the Office's allegation that the term "reactive" is indefinite. Reactive is understood by those having ordinary skill in the art to mean, in the context of the instant application, the ability of an antibody or other biological or synthetic composition to recognize and/or interact with the subject polypeptides. Such an understanding of the word reactive is implicit in the specification at, for example, page 3, lines 9-12, and further suggested by page 7, lines 12-15.

Claim 9 has been amended to recite the proper antecedent basis, "polypeptide" rather than "protein." The Office alleges that claims 9, 10, and 11 are indefinite for omitting essential elements, such as certain method steps and refers to M.P.E.P. § 2172.01 as support for this proposition. However, the language in § 2172.02 of the M.P.E.P., on which the Office relies, is directed to the enablement requirement rather than the indefiniteness requirement as set forth by the Office. Therefore, an indefiniteness rejection for the claimed subject matter is not proper according to the M.P.E.P. Furthermore, an enablement rejection is also improper for claim 9. Enablement must viewed from the perspective of one having ordinary skill in the art, and the assessment of the amount of experimentation required to practice the claimed invention. With respect to the instant application, a skilled artisan would be able to practice the claimed methods without undue experimentation since purifying polypeptides using antibodies is a well know technique in the molecular biology arts. Additionally, the Office alleges that claim 9 is indefinite because it is unclear which antibody is being used in the method. Likewise, this element of claim 9 satisfies the requirement for definiteness as found in the M.P.E.P. § 2173.02, which states that "[d]efinitness of claim language must be analyzed, not in a vacuum, but in light of: (A) The content of the particular

application disclosure; (B) The teachings of the prior art; and (C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made." With respect to the definiteness of the antibody being used to carry out the method of claim 9, one having ordinary skill in the art would understand that any antibody recognizing the subject polypeptides can be used to carry out the inventive methods.

The Office alleges that claim 10 is also indefinite for attempting to contact cells after they have been solubilized. On page 4 of the Office Action, the Office states that "it is impossible to contact said *cells* after solubiliztion, as said 'cells' would not exist anymore." However, the Office goes on to directly contradict its position in its discussion of the Cerretti and Colamonici references, which are cited as prior art to the instant application. Specifically, the Office states that Cerretti et al. discloses "a method for purifying the polypeptide by using an antibody.....wherein the method involves solubilization of the cells, contacting with said antibody...and eluting." *See* Page 5, Office Action of June 3, 2004. Although the Office alleges the subject matter of claim 10 is "impossible," later cited art describes a similar technique to reach a similar outcome – the purifying of a polypeptide. Accordingly, the language of claim 10, when viewed in light of the prior art, particularly points out and distinctly claims the inventive method.

Claim 12 has been amended to recite the proper antecedent basis, "anti-interleukin-2 receptor associated polypeptide" rather than "anti-ILRAP." Claim 13 has also been amended to recite the proper antecedent basis from claim 9, wherein amended claim 13 recites "interleukin-2 receptor" rather than "interleukin-2." Claim 13 also has been amended to correct a typographical omission from the term "interleukin β subunits," wherein the claim now recites "interleukin-2Rβ subunits" as supported by the specification at, for example, page 26, line 24. Accordingly, the amendments to claims 12 and 13 render moot the indefiniteness rejections with respect to these claims.

In view of the foregoing, Applicants submit that claims 1, 3-5, and 9-15 particularly point out and distinctly claim Applicants invention. Therefore, Applicants respectfully request that the rejection of claims 1, 3-5, and 9-15 for allegedly being indefinite be withdrawn.

Discussion of Rejections under U.S.C. § 102

In the instant application, amended claims 1 and 3 recite molecular weight limitations for the subject polypeptides, wherein the weight limitations are determined by SDS-PAGE. The molecular weight of the polypeptides recited in claims 1 and 3 is 32,000 to 34,000

daltons and 26,000 to 28,000 daltons, respectively, as determined by SDS-PAGE. The polypeptide(s) disclosed in Cerretti et al. have a molecular weight ranging from 55,000 to 60,000 daltons as determined by SDS-PAGE. *See* Cerretti et al. at page 10, and page 26, Example 6. A single prior art reference must disclose each and every limitation of a claimed invention, either explicitly or inherently, to anticipate the claimed invention. *Mehl/Biophile Int'l Corp. v. Milgraum*, 192 F.3d 1362, 1365 (Fed. Cir. 1999). The molecular weight of the subject polypeptides is not disclosed in Cerretti et al., and there is no additional evidence cited by the Office or in Cerretti et al. that one having ordinary skill in the art could rely upon to conclude that the polypeptides disclosed in Cerretti et al. anticipate the subject polypeptides of the instant application. Cerretti et al. does not disclose, explicitly or inherently, all the limitations of claims 1 and 3-5 and, therefore, fails to anticipate these claims.

The methods described in claims 9-15 are not anticipated by Cerretti et al. Cerretti et al. discloses the purification of an IL-2R subunit, specifically, the IL-2Rα subunit. It is well know in the art that the IL-2 receptor comprises three subunits, α, β, and γ. *See* Janeway et al., Immunobiology 5, p.313 (2001) (excerpt enclosed herewith). Thus, one of ordinary skill in the art would not define the relationships between the receptor subunits as "associating" with the IL-2 receptor, but rather as the IL-2 receptor itself. That is, one having ordinary skill in the art would differentiate the subunits forming a composition from separate and distinct molecules, such as a polypeptides, that associate with said composition. Thus, Cerretti's IL-2R (IL-2Rα subunit) does not meet the definition of an "IL-2R associated polypeptide" as defined by the instant specification. As such, Cerretti et al. does not meet the limitations of claims 9-15, either explicitly or inherently, and, therefore, fails to anticipate those claims.

The Office alleges that Colamonici et al. anticipates under § 102(b), or renders obvious under § 103(a), claims 1, 3-5, 9, 10, and 13-15 of the instant application. Like Cerretti et al, Colamonici et al. does not teach an "associated" polypeptide as defined by the instant specification.

An allegation of anticipation can be refuted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. *In re Best*, 562 F.2d 1252, 1255, 195 U.S.P.Q. 430, 433 (C.C.P.A. 1977). Colamonici et al. briefly recites "It is worth noting that two other bands with molecular mass of 37 and 20 kDa...and some times a 42 kDa band were present...." First, the molecular mass of any polypeptide identified in Colamonici et al. does not fall with in the range of molecular mass recited for either of the subject polypeptides, 32 – 34 kDa and 26 – 28 kDa, even though the same technique (SDS-

PAGE) was used to determine molecular mass. Second, the bands do not necessarily possess the characteristics of the claimed product as evinced by Colamonici et al. Colamonici et al. states that, "These bands might correspond to 2, or even 3 novel proteins," and that it is possible that these bands (20 kDa and 37 kDa) correspond to degradation products of the 55 kDa protein (IL-2Rα-subunit). Thus, Colamonici et al. itself, demonstrates that the prior art does not necessarily possess the characteristics of the claimed product.

The Office also alleges claims 14 and 15 recite a limitation for "a composition," which is met by the disclosure of Colamonici et al. However, Applicants point out that no limitation for "a composition is recited in claim 14, 15, or any claim from which they depend.

In view of the foregoing, Applicants submit that claim 1, 3-5, and 9-15 particularly are not anticipated by the cited art. Therefore, Applicants respectfully request that the rejection of claims 1, 3-5, and 9-15 as allegedly anticipated be withdrawn.

Discussion of Rejections under U.S.C. § 103

The Office asserts that claims 1, 3-5, and 9-15 are allegedly obvious in view of Cerretti et al. and Colamonici et al. In order to establish a *prima facie* case of obviousness, the Office must identify each and every element of the claimed invention in one or more references. *See In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991). The Office has not met its burden in establishing a prima facie case of obviousness. Accordingly, Applicants traverse.

Neither Cerretti et al. nor Colamonici et al. disclose an interleukin-2 receptor associated polypeptide, as recited in the claims, and as defined by the instant specification, and therefore, Cerretti et al. does not cure the deficiencies of Colamonici et al. or vice versa. Likewise, with respect to claims 1 and 3-5, neither reference describes a polypeptide within the molecular mass range recited for either subject polypeptide, such that the prior art references relied upon by the Office do not teach or suggest all of the elements of the claims. Accordingly, Applicants hereby request that the rejection of claims 1, 3-5, and 9-15 as allegedly obvious be withdrawn.

Finally, the Office relies on a rejection described as 35 U.S.C. §§ 102/103, citing Cerretti et al. evidenced by Colamonici et al. This type of rejection is appropriate when the prior art is silent as to a limitation of the subject claims, however, inherently possess said limitation. *See* M.P.E.P. § 2112. The burden is on the Examiner to provide rationale or evidence that makes clear that the missing limitation is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Id. However, the fact that a certain characteristic <u>may</u> be present in the prior art is not sufficient

to establish inherency of that characteristic. *See In re Rijckaert*, 9 f.3d 1531, 1534, 28 U.S.P.Q.2d 1955, 1957 (Fed. Cir. 1993).

The Examiner has not mentioned the concept of inherency, let alone described how the subject claims can be regarded as inherent in the cited art, Moreover, the Examiner provided any rationale or evidence demonstrating that said characteristic necessarily flows from the cited references. As discussed above, the cited references do not anticipate the subject claims because the references do not recite all of the limitations of the claims as amended, namely the molecular weight of subject polypeptides. Furthermore, there is no motivation or suggestion for one of ordinary skill in the art to limit the molecular weight of the subject polypeptides to the ranges recited herein; thus, rendering the claims non-obvious in view of the cited references. Therefore, the Examiner has not met the burden for rejecting the instant claims under 35 U.S.C. § § 102/103, which requires a showing that a limitation of the claim is inherent in the prior art. Accordingly, Applicants traverse this rejection.

Conclusion

The application is considered in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

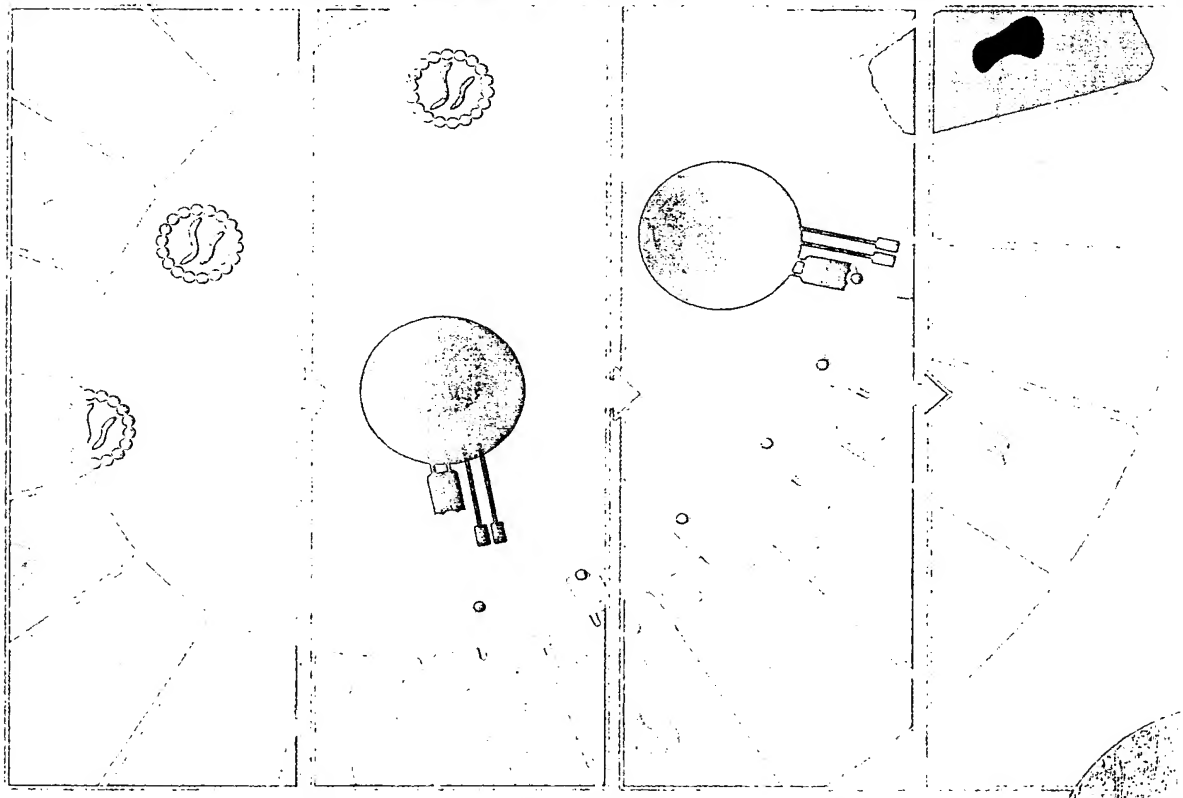
Respectfully submitted,

David J. Schodin, Reg. No. 41,294
LEYDIG, VOIT & MAYER, LTD.
Two Prudential Plaza, Suite 4900
180 North Stetson Avenue
Chicago, Illinois 60601-6780
(312) 616-5600 (telephone)
(312) 616-5700 (facsimile)

Date: September 3, 2004

immunobiology 5

THE IMMUNE SYSTEM IN HEALTH AND DISEASE



FIFTH EDITION

animated
cd-rom inside

CHARLES A JANEWAY • PAUL TRAVERS
MARK WALPORT • MARK SHLOMCHIK

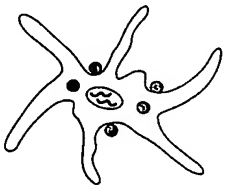
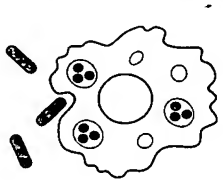
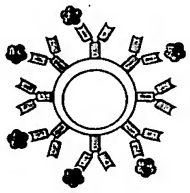
	Dendritic cells	Macrophages	B cells
			
Antigen uptake	+++ Macropinocytosis and phagocytosis by tissue dendritic cells Viral infection	Phagocytosis +++	Antigen-specific receptor (Ig) ++++
MHC expression	Low on tissue dendritic cells High on dendritic cells in lymphoid tissues	Inducible by bacteria and cytokines – to +++	Constitutive Increases on activation +++ to ++++
Co-stimulator delivery	Constitutive by mature, nonphagocytic lymphoid dendritic cells ++++	Inducible – to +++	Inducible – to +++
Antigen presented	Peptides Viral antigens Allergens	Particulate antigens Intracellular and extracellular pathogens	Soluble antigens Toxins Viruses
Location	Lymphoid tissue Connective tissue Epithelia	Lymphoid tissue Connective tissue Body cavities	Lymphoid tissue Peripheral blood

Fig. 8.18 The properties of the various antigen-presenting cells. Dendritic cells, macrophages, and B cells are the main cell types involved in the initial presentation of foreign antigens to naive T cells. These cells vary in their means of antigen uptake, MHC class II expression, co-stimulator expression, the type of antigen they present effectively, their locations in the body, and their surface adhesion molecules (not shown).

8-9 Activated T cells synthesize the T-cell growth factor interleukin-2 and its receptor.

Naive T cells can live for many years without dividing. These small resting cells have condensed chromatin and a scanty cytoplasm and synthesize little RNA or protein. On activation, they must reenter the cell cycle and divide rapidly to produce the large numbers of progeny that will differentiate into armed effector T cells. Their proliferation and differentiation are driven by a cytokine called **interleukin-2** (IL-2), which is produced by the activated T cell itself.

The initial encounter with specific antigen in the presence of the required co-stimulatory signal triggers entry of the T cell into the G_1 phase of the cell cycle; at the same time, it also induces the synthesis of IL-2 along with the α chain of the IL-2 receptor. The IL-2 receptor has three chains: α, β, and γ (Fig. 8.19). Resting T cells express a form of this receptor composed of β and γ chains which binds IL-2 with moderate affinity, allowing resting T cells to respond to very high concentrations of IL-2. Association of the α chain with

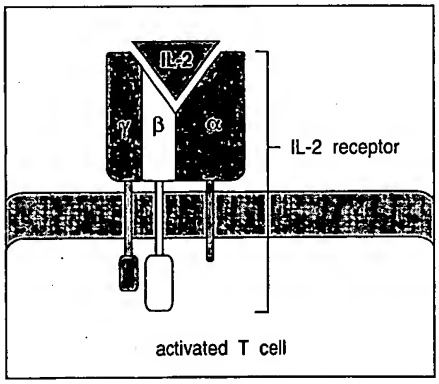


Fig. 8.19 High-affinity IL-2 receptors are three-chain structures that are produced only on activated T cells. On resting T cells, the β and γ chains are expressed constitutively. They bind IL-2 with moderate affinity. Activation of T cells induces the synthesis of the α chain and the formation of the high-affinity heterotrimeric receptor. The β and γ chains show similarities in amino acid sequence to cell-surface receptors for growth hormone and prolactin, both of which also regulate cell growth and differentiation.